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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/801,087	03/15/2004	Rudolph E. Tanzi	M0765.70052US01	2184
23628 7590 02/07/2007 WOLF GREENFIELD & SACKS, PC FEDERAL RESERVE PLAZA 600 ATLANTIC AVENUE BOSTON, MA 02210-2206			EXAMINER BALLARD, KIMBERLY A	
			ART UNIT	PAPER NUMBER
			1649	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/07/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

10/801,087

Applicant(s)

TANZI ET AL.

Examiner

Kimberly A. Ballard

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 November 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 23,26,28,31 and 52-56 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 23,28,31,52,53,55 and 56 is/are rejected.
- 7) ☒ Claim(s) 26 and 54 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of Application, Amendments and/or Claims

In the response filed November 13, 2006, claims 1-3, 5, 8, 12-14, 16, 18, 19, 23, 26, 28, 31-34, 36, 38 and 39 have been canceled and claims 52-56 have been added. Claims 23, 26, 28, 31 and 52-56 are pending.

Claims **23, 26, 28, 31** and **52-56** are under examination in the instant office action.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Claim Rejections

The rejection of claims 23, 28, and 31 under 35 U.S.C. 112, first paragraph (written description), as set forth at pp. 6-8 of the previous office action (05/09/2006) is withdrawn in view of Applicant's arguments.

Maintained and New Claim Objections/Rejections, Necessitated by Amendment

Claim Rejections - 35 USC § 112, 1st Paragraph

Claims 23, 28, 31 and newly added claims 52, 53, 55 and 56 are rejected under 35 U.S.C. 112, first paragraph, for reasons of record as set forth in the previous office action (05/09/2006) because the specification, while being enabling for a method for

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identifying compounds that modulate caspase activation-induced stabilization of presenilins, nicastrin/Aph2, BACE, Aph1a, and Pen-2, *does not reasonably provide enablement for* identifying compounds that modulate caspase activation-induced stabilization of all secretase pathway associated proteins as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In the response filed November 9, 2006, Applicant argues that the skilled artisan would not be required to undertake undue experimentation to practice the claimed invention for the following reasons: 1) the prior art provides additional secretase pathway associated proteins in addition to those enumerated in the specification, and therefore the identification of such proteins would not be considered to require undue experimentation; and 2) methods for determining the stability of a protein, such as a secretase pathway associated protein, were well known in the prior art, such that only a small and routine quantity of experimentation is required to determine if a particular secretase pathway associated protein is stabilized by caspase activation.

Applicant's arguments have been fully considered but they are not persuasive. As noted previously, the claims are broadly drawn to a method for identifying compounds that modulate caspase activation-induced stabilization of a secretase pathway associated protein, wherein the method requires measuring the stability of the secretase pathway associated protein. The specification broadly defines a "secretase pathway associated protein" as a protein that is involved in the production of A β from

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amyloid precursor protein (APP) and is inclusive of, but not limited to: presenilins (including PS1 and PS2), nicastrin/Aph2, Aph1a, Pen-2, and BACE. However, the list of secretase molecules provided in the instant application is far from complete. It is noted that the definition of secretase pathway associated protein is open-ended, because any number of proteins may be involved in varying degrees in the production of A β .

The prior art cited in the previous office action was provided to demonstrate the unpredictability of deciphering the particular molecules involved in secretase processing of A β , as the relevant literature notes that there are still *as-yet-undefined* secretases as well as proteins that modulate secretase proteins – all of which would qualify as “secretase pathway associated proteins”. Thus, the skilled artisan would have to first reliably identify these secretase pathway associated proteins and their role in the pathway before the artisan could practice the method of determining modulators of caspase activation-induced stabilization, which would constitute undue experimentation. Moreover, it is unclear whether any of these other known or as-yet-unknown secretase pathway associated proteins would be relevant to the instant invention, that is, whether a difference in their stability due to a modulator would make any difference in the production of A β or some other desired outcome. The artisan would thus require further guidance regarding the role/function of the newly discovered secretase pathway associated protein so as to determine the benefits of increasing or decreasing the protein’s stability. As such, if the role of the novel protein in the secretase pathway is unknown, the skilled artisan would have to undertake additional experimentation to

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establish whether modulation of its stability would be at all advantageous. Thus, while the skilled artisan may be able to identify and determine if a particular secretase pathway associated protein is stabilized by caspase activation, the protein's stability (or lack thereof) may have no measurable effect on A β processing. The addition of new claims 52 and 53 substantiates that the instant claims are not enabled for the full scope of the invention because claims 52-53 essentially allow the skilled artisan to practice unlimited experimentation in the identification of both inhibitors and enhancers of stability of the secretase pathway associated protein, whose role in the secretase pathway may not yet be established.

In summary, it would not be expected that one of ordinary skill in the art could successfully practice the instant invention as broadly claimed for the reasons stated above. When combined with the lack of guidance from the instant specification on secretase pathway associated proteins and the state of the art which suggests unpredictability in the identification of additional secretase proteins and their involvement in A β processing, the claims merely represent an invitation to experiment to discover how to use Applicants' invention.

Claim Objections

Applicant is advised that should claim 23 be found allowable, claim 56 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing

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one claim to object to the other as being a substantial duplicate of the allowed claim.

See MPEP § 706.03(k). Claim 56 recites that the cells are contacted with the candidate modulator after caspase activation induction, however, claim 23 already recites "contacting cells that have been induced to undergo caspase activation with a candidate modulator". Thus, the method of claim 23 requires that the cells have already been induced to undergo caspase activation before they are contacted with a candidate compound.

Claims 26 and 54 are objected to because they depend from rejected claim 23.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 53 and 55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 53 recites the limitation "a decrease of the protein" in line 1 which renders the claim indefinite. Firstly, there is insufficient antecedent basis for this limitation in the claim. Claim 23, from which claim 53 depends, recites measuring the *stability* of a secretase pathway associated protein, not measuring the protein itself. Secondly, it is unclear what is being measured by a "decrease of the protein" – i.e., protein amount?

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Phosphorylation? Protein stability? Finally, it is unclear how to compare a “decrease [in] protein” to a “stability of the protein”, as these may be different types of measurements. Based on these reasons, the metes and bounds of the claim cannot be ascertained.

Claim 55 is ambiguous and indefinite because it recites that the cells “are contacted with the candidate modulator before caspase activation induction.” Claim 23, however, recites a “method for identifying compounds that modulate caspase activation-induced stabilization of a secretase pathway associated protein”. The preamble of claim 23 thus implies that the modulation of stabilization is subsequent to caspase activation induction. It is therefore unclear how to identify such a modulator of a protein whose stabilization is caspase activated when the cells have not yet been induced to undergo caspase activation. The metes and bounds of the claim thus cannot be ascertained.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly A. Ballard whose telephone number is 571-272-4479. The examiner can normally be reached on Monday-Friday 9AM - 5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Kimberly Ballard, Ph.D.
January 29, 2007

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER